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Proposed collaboration between JPL and the Healthcare system to address stress disorders

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What we know about stress

- Human stress response originates in the Hypothalamic-Pituitary-Adrenal (HPA) axis.
- For humans the need to maintain HPA-axis stability is supported by successive layers of feedback systems that can exert complementary stabilizing influences.
- Much is known about the regulatory processes involving system parameters that stabilize cortisol rhythmicity on the cellular/molecular level.
- We know less about parametric influences operating on other levels of scale, including at the cognitive level of thought and perception, individual behavior, social behavior, or community and political behavior.
- Astronaut Scott Kelly's epigenetic DNA expression has changed by 7% due to his year-long stay in the international Space Station, and significant attention is being given to DNA methylation as a health consideration related to space flight.
- Methylation of DNA in the HPA-Axis is responsible for increased stress reactivity and chronic activation of immune inflammatory response, which is known to significantly contribute to early onset of chronic diseases and early death.

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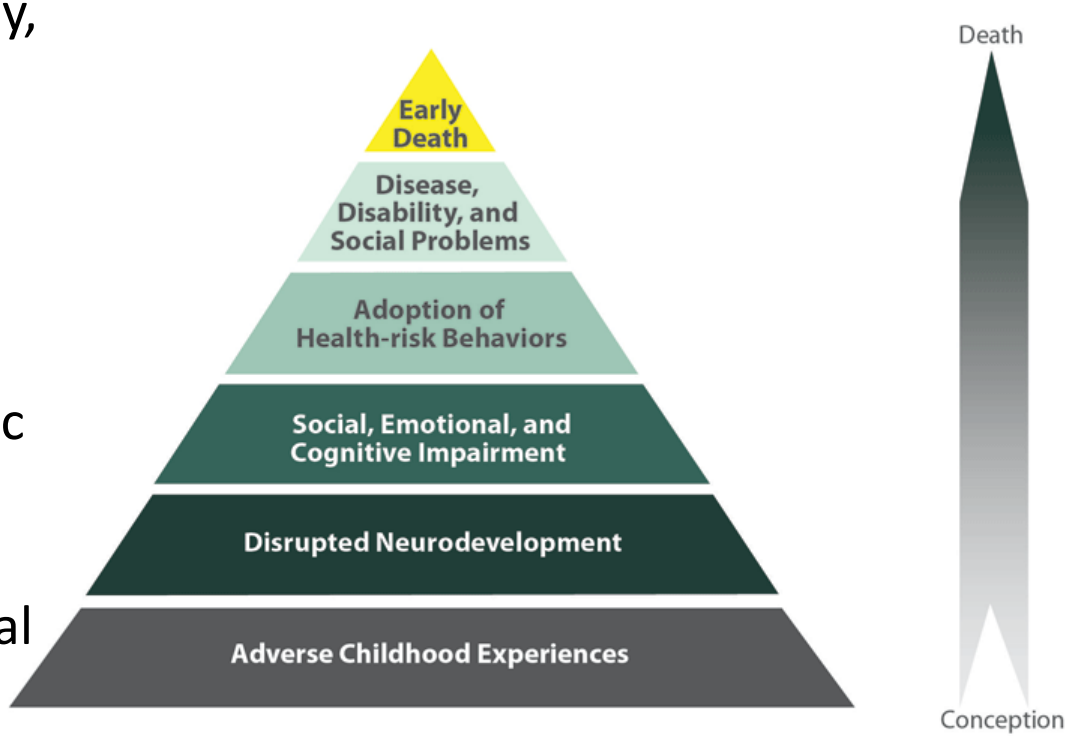
Connection between cortisol rhythmicity and health care

- Vincent Felitti's, M.D., pioneering work in the now famous ACE Study, which explores the impact of trauma during childhood has resulted in assessment tools and predictive models for a wide variety of health and behavioral outcomes related to early-life toxic stress and trauma.

- These models point to neurological changes that are now understood to reflect the results of DNA methylation on set point in the HPA-Axis, the stress center of the brain.



Mechanism by Which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

ACE Study – CDC-Kaiser – 17,000 patients - http://www.cdc.gov/violenceprevention/acestudy/about.html

There is a critical need for a computer model of the cortisol cycle in the HPA-axis to understand stress response across scales

- Cortisol rhythmicity displays identifiable nonlinear properties, which suggests the operation of a nonlinear system
- Effective regulation is important to keep the rhythm stable
- It is important to develop a better understanding of how all of the above works because a lot of cost to healthcare and society is riding on our ability to develop solutions.
- Multiscale modeling and simulation of cortisol rhythmicity can be accomplished by nonlinear dynamical system techniques.
- These strategies involve the use of powerful mathematical tools and related concepts that JPL applies to space flight and high-level engineering problems. Also, nonlinear systems can be modeled in a computer, allowing us to study how they work.

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NASA proposal opportunity

TRANSLATIONAL RESEARCH INSTITUTE FOR SPACE HEALTH

About the Solicitation	**TRISH** is seeking and funding emerging scientific and **Biomedical Research Advances for Space Health (BRASH)**, disruptive technologies, therapies, and new approaches that reduce risks to human health and performance during deep space exploration. Annual budget up to $400,000 with a project duration of 2 years
Areas of Interest	BRASH solicitation is solely focused on the following six topics: Predictive algorithms of health, behavior, and medical events Improving resilience through nucleotide-based therapy Non-pharmacological improvement of human performance Multipurpose edible plants for spaceflight applications New materials for shielding medications Test your expired medications
Schedule	The solicitation is composed of 4 phases. Phase 1 includes the release, pre-proposal webinar, and three-page proposal (Step-1). In Phase 2, select Step-1 proposers will be invited to submit a full-length Step-2 proposal. In Phase 3 proposals are reviewed for scientific, technical, and programmatic merit. Awardees are notified in Phase 4. **March 16, 2018** BRASH 1801 Release **April 27, 2018** Step-1 Notifications **June 25, 2018** 5:00 pm EST Step-2 Proposals Due **November 2018** Selection Announcement STEP-1 → STEP-2 → REVIEW → SELECTION **March 28, 2018** 2-3:00 pm EST Pre-Proposal Webinar **April 16, 2018** 5:00 pm EST Step-1 Proposals Due
About TRISH	At TRISH, we focus on approaches that NASA needs and is not currently pursuing. We seek high risk, high reward, high quality and efficient solutions that can be adapted (or translated) for use in space. Cool, right?! Find out more information about TRISH at bcm.edu/spacehealth.
Why TRISH?	TRISH offers: Non-dilutive federal funding Access to spaceflight and space analogs New partnerships through our virtual network High risk threshold
Eligibility	Personnel employed by U.S.-based institutions or companies may apply. All organizations must register (or already be registered) with the System for Award Management (SAM).
Contact	Questions regarding BRASH1801? Not sure whether or how your research could apply to the challenges astronauts face in space? We can help! Contact emmanueo@bcm.edu about BRASH1801 or to learn about other TRISH funding opportunities.

preliminary - for discussion purposes only

Specific Aims

- Evaluate the ACE Score model as a screening resource for prospective astronauts and expand application of basic concepts to develop assessment tools for adult-experienced trauma such as might occur during space missions.

- Develop/adapt mathematical and computer models that describe the effects of stress and trauma on circadian and ultradian rhythmicity in the HPA-Axis, including attractor-state instabilities and pathways for resilience that may result from multi-layered parametric influences.

- Propose a prevention, resilience, and recovery paradigm that builds on insights gained from studying centenarians in the Blue Zone longevity project at Loma Linda University, especially those who have high ACE Scores and have enjoyed good health, nonetheless.

Cohorts

- Three cohorts will be identified.
- Two cohorts will be recruited from among the approximately 4000 super-utilizers (patients with complex-care needs who are frequently seen in the emergency department or admitted to the hospital and who appear to display toxic stress or trauma-related behavior and health outcomes as predicted by the ACE-Score algorithm) that have been identified at Adventist Health Glendale.
- The first of these cohorts will be super-utilizers with high ACE Scores.
- The second cohort will include adults whose precipitating toxic stress or trauma occurred in adulthood.
- The third cohort will include subjects of great longevity currently being studied in the Blue-Zone project at Loma Linda University.

Proposed collaborating Institutions and Partners

- Jet Propulsion Laboratory – California Institute of Technology (JPL)
- Loma Linda University (LLU)
- Adventist Health Glendale (AHGL)
- California Institute of Preventive Medicine (Vincent Felitti)
- UCLA Cousins Center for Psychoneuroimmunology, (Steve Cole)
- Duke University Center for Spirituality, Theology and Health (Harold Koenig)

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Summary of multiscale stability factors in HPA-Axis in humans

Layers of Influence	Regulatory Process (Rule Sets that drive self-organization)	Pathology	Agency	Maintaining & Restoring Stability
Molecular (Intrinsic)	Genetic	HPA-axis instability via cortisol and beta-endorphin rhythmicity,	Epi-genetics- Methylation, Etc.	Pharmacological Agent(s)
Cellular (Intrinsic)	Immune System, Hormonal Operations, Etc.	Various Disease states: • Inflammatory Process, • Cell Injury & Death,	Physiological Systems	Physical Medicine
Cognitive (Extrinsic)	Rationality (Logic)	Cognitive Distortions, Mental Illness	Neurological Systems	Behavioral Medicine, Mental Health Therapist,
Behavioral (Extrinsic)	Core Values, Personal Code	Lack of Self-control Impulsivity, Stress Reactivity	Individuals	Self + Resources Below
Family (Extrinsic)	Oral & Written Rules, Family Traditions	Divorce, Abandonment, Juvenile Delinquency	Family Systems	Parents, Grand Parents, Relatives
Social (Extrinsic)	Social Conventions, Manners & Respect, Ethics	Incivility, Discourtesy, Bullying	Friends, Social Groups,	Peer Pressure, Group Influence
Community (Extrinsic)	Contracts & Agreements Corporate Governance, Policy & Regulations,	Poverty, Ignorance, Inequity	Business and Commerce, Coalitions, Cooperatives	Civil Law Systems, Schools, Churches,
City, County, State, Federal (Extrinsic)	Charters & Constitutions, Codes, Ordinances, & Laws	Violations of Law, Crime	Governments via Law Enforcement,	Criminal Law via Justice system
Geo-Political (Extrinsic)	Treaties, International Law,	Conflict & Hostilities, War,	Nation States via Militaries,	United Nations International Law Court, Tribunals